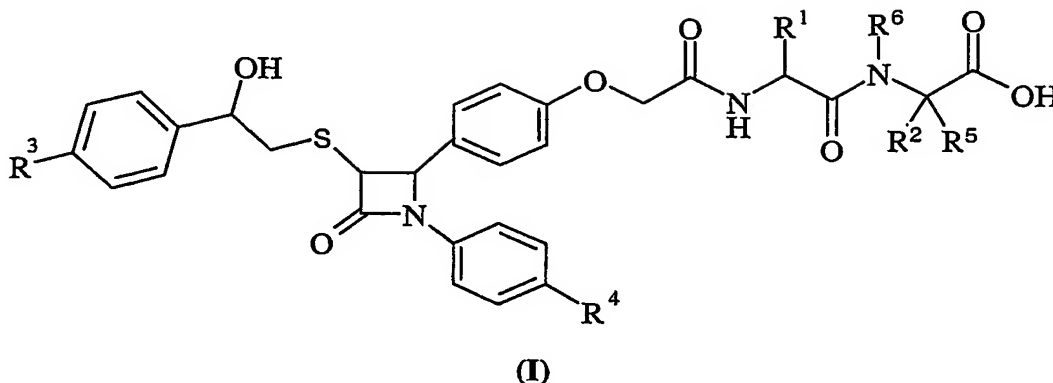


Claims

1. A compound of formula (I):



wherein:

R^1 is hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl or aryl; wherein said C_{1-6} alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6} alkoxy, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl) $_2$ amino, C_1 - C_6 alkylcarbonylamino

- 10 C_{1-6} alkylS(O) $_a$ wherein a is 0-2, C_{3-6} cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6} alkyl or C_{1-6} alkoxy;

R^2 and R^5 are independently hydrogen, a branched or unbranched C_{1-6} alkyl, C_{3-6} cycloalkyl or aryl; wherein said C_{1-6} alkyl may be optionally substituted by one or more hydroxy, amino,

- 15 guanidino, cyano, carbamoyl, carboxy, C_{1-6} alkoxy, aryl C_{1-6} alkoxy, $(C_1-C_4)_3Si$, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl) $_2$ amino, C_{1-6} alkylS(O) $_a$, C_{3-6} cycloalkyl, aryl or aryl C_{1-6} alkylS(O) $_a$, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6} alkyl or C_{1-6} alkoxy;

R^3 is hydrogen, alkyl, halo, C_{1-6} alkoxy or C_{1-6} alkylS-;

- 20 R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6} alkoxy;

R^6 is hydrogen, C_{1-6} alkyl, or aryl C_{1-6} alkyl;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

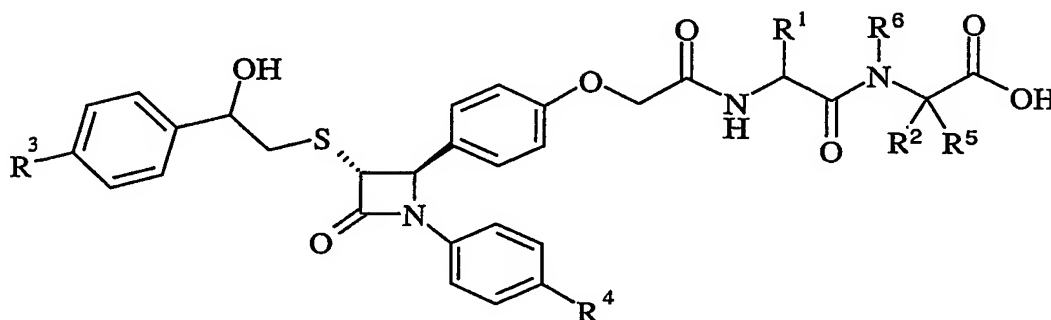
or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

- 25 with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(N -(N -(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl} carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-

2-hydroxyethylsulphonyl]-4-{4-[*N*-((*R*)- α -{*N*-[(*S*)-1-(carboxy)-2-(hydroxy)ethyl]carbamoyl}benzyl)carbamoylmethoxy]phenyl}azetidin-2-one.

2. A compound of formula (I2):

5



(I2)

wherein:

- R¹** is hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C₁₋₆alkoxy, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁-C₆ alkylcarbonylamino C₁₋₆alkylS(O)_a wherein a is 0-2, C₃₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;
- R²** and **R⁵** are independently hydrogen, a branched or unbranched C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C₁₋₆alkoxy, aryl C₁₋₆alkoxy, (C₁-C₄)₃Si, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkylS(O)_a, C₃₋₆cycloalkyl, aryl or aryl C₁₋₆alkylS(O)_a, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;
- R³** is hydrogen, alkyl, halo, C₁₋₆alkoxy or C₁₋₆ alkylS-;
- R⁴** is hydrogen, C₁₋₆ alkyl, halo or C₁₋₆alkoxy;
- R⁶** is hydrogen, C₁₋₆ alkyl, or arylC₁₋₆ alkyl;
- wherein **R⁵** and **R²** may form a ring with 2-7 carbon atoms and wherein **R⁶** and **R²** may form a ring with 3-6 carbon atoms;
- or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(N-{N-[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylemethyl} carbamoylemethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-{4-[N-((R)- α -{N-[(S)-1-(carboxy)-2-(hydroxy)

5 ethyl]carbamoylemethyl}benzyl)carbamoylemethoxy]phenyl}azetidin-2-one.

3. A compound according to claim 1 or 2, wherein:

R¹ is hydrogen or phenyl.

10 4. A compound according to any of the preceding claims, wherein:

R² is hydrogen, a branched or unbranched C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, acylamino, C₁₋₆alkylS(O)_a wherein a is 0-2, C₃₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by hydroxy, alkyl, alkoxy or cyano.

15

5. A compound according to any of the preceding claims, wherein:

R³ is hydrogen, C₁-C₂alkyl, halo or methoxy.

6. A compound according to any of the preceding claims, wherein:

20 **R³** is hydrogen, methyl, chlorine, fluorine, C₁₋₆ alkylS-, or methoxy.

7. A compound according to any of the preceding claims, wherein:

R⁴ is hydrogen or halo.

25 8. A compound according to any of the preceding claims, wherein:

R⁴ is chlorine or fluorine.

9. A compound according to any of the preceding claims, wherein:

R⁶ is hydrogen, C₁₋₆ alkyl, arylC₁₋₆alkyl or **R⁶** and **R²** form a ring with 3-6 carbon atoms.

30

10. A compound according to claim 1, wherein:

R¹ is hydrogen;

R^2 is a branched or unbranched C_{1-4} alkyl, optionally substituted by a C_{3-6} cycloalkyl, alkylS-, aryl optionally substituted by hydroxy or cyano, amino, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl)₂amino or aryl C_{1-6} alkylS(O)_a, wherein a is 0-2

5 R^3 and R^4 are halo;

R^5 is hydrogen or C_{1-6} alkyl; and

R^6 is hydrogen.

11. One or more compounds chosen from:

10 N -{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl- N^6 -acetyl-D-lysine;

1-(4-Fluorophenyl)-3-(*R*)-[2-(4-fluorophenyl)-2-hydroxyethylthio]-4-(*R*)-{4-[N -{ N -[2-(phenyl)-1-(*R*)-(carboxy)ethyl]carbamoylethyl]carbamoylethoxy]phenyl}azetidin-2-one;

15

N -{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-valine;

N -{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-

20 oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-tyrosine;

N -{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-proline;

25 N -{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-lysine;

N -{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-hydroxy-2-(4-methoxyphenyl)ethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-D-valine;

30

N -{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-2-butylnorleucine;

N-{[4-((2*R*,3*R*)-1-(4-Fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-*S*-methyl-*L*-cysteine;

- 5 *N*-{[4-((2*R*,3*R*)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-cyclohexyl-*D*-alanine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-cyclohexyl-*D*-alanine;

10

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-4-methylleucine;

N-{[4-((2*R*,3*R*)-1-(4-Fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-

- 15 oxoazetidin-2-yl)phenoxy]acetyl}-*L*-alanyl-*D*-valine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-hydroxy-2-(4-methylphenyl)ethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-*D*-valine;

- 20 *N*-{[4-((2*R*,3*R*)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-*D*-valine;

N-{[4-((2*R*,3*R*)-1-(4-chlorophenyl)-3-{[2-(4-chlorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-methyl-*D*-valine;

25

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-(2-naphthyl)-*D*-alanine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-

- 30 oxoazetidin-2-yl)phenoxy]acetyl}glycyl-3-methyl-*D*-valine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-(3*R*,4*S*,5*R*)-3,4,5,6-tetrahydroxy-*D*-norleucine.

N-{[4-((2*R*,3*R*)-1-(4-Fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-*N*,2-dimethylalanine

5 *N*-({4-[(2*R*,3*R*)-1-(4-Fluorophenyl)-3-({2-hydroxy-2-[4-(methylthio)phenyl]ethyl}thio)-4-oxoazetidin-2-yl]phenoxy}acetyl)glycyl-3-methyl-D-valine

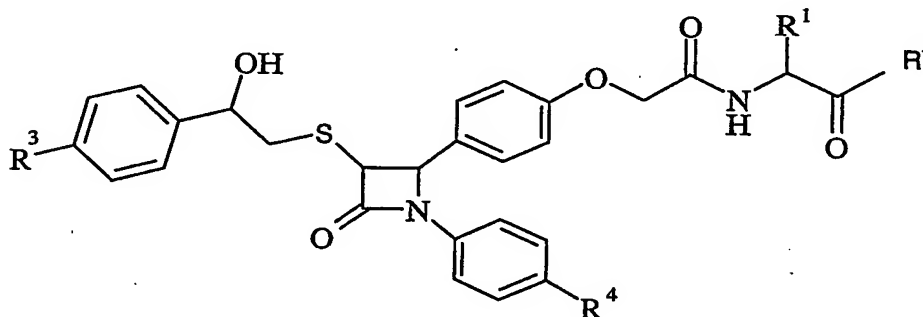
N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-*S*-(4-methylbenzyl)-D-cysteine

10 *N*-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-*S*-(*tert*-butyl)-D-cysteine

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-{[2-(4-fluorophenyl)-2-hydroxyethyl]thio}-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl-*b*,*b*-dimethyl-D-phenylalanine.

15

12. A compound of the formula (XV) or hydrolysable esters or amides thereof:



20

(XV)

wherein:

R^1 is hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl or aryl; wherein said C_{1-6} alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy,

25 C_{1-6} alkoxy, *N*-(C_{1-6} alkyl)amino, *N,N*-(C_{1-6} alkyl)₂amino, C_1 - C_6 alkylcarbonylamino C_{1-6} alkylS(O)_a wherein a is 0-2, C_{3-6} cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6} alkyl or C_{1-6} alkoxy;

- R^2 and R^5 are independently hydrogen, a branched or unbranched C_{1-6} alkyl, C_{3-6} cycloalkyl or aryl; wherein said C_{1-6} alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6} alkoxy, aryl C_{1-6} alkoxy, $(C_1-C_4)_3Si$, $N-(C_{1-6}alkyl)amino$, $N,N-(C_{1-6}alkyl)_2amino$, $C_{1-6}alkylS(O)_a$, aryl $C_{1-6}alkylS(O)_a$, wherein a is 0-2, C_{3-6} cycloalkyl or
- 5 aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6} alkyl or C_{1-6} alkoxy;
- R^3 is hydrogen, alkyl, halo, C_{1-6} alkoxy or $C_{1-6}alkylS-$;
- R^4 is hydrogen, $C_{1-6}alkyl$, halo or $C_{1-6}alkoxy$;
- R^6 is hydrogen, $C_{1-6}alkyl$, or aryl $C_{1-6}alkyl$;
- 10 R^7 is an hydroxy group or a $C_{1-3}alkoxy$ group;
- wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;
- or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;
- with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-
- 15 hydroxyethylsulphanyl]-4-[4-(N -{ N -[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl} carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-
- 2-hydroxyethylsulphanyl]-4-{4-[N -((R)- α -{ N -[(S)-1-(carboxy)-2-(hydroxy) ethyl]carbamoyl}benzyl)carbamoylmethoxy]phenyl}azetidin-2-one.
- 20 13. A method of treating or preventing hyperlipidemic conditions comprising the administration of an effective amount of a compound according to any one of claims 1 to 12 to a mammal in need thereof.
14. A method of treating or preventing atherosclerosis comprising the administration of an
- 25 effective amount of a compound according to any one of claims 1 to 12 to a mammal in need thereof.
15. A method for treating or preventing Alzheimers' disease comprising the administration of an effective amount of a compound according to any one of claims 1 to 12 to a mammal in
- 30 need thereof.

16. A method for treating or preventing cholesterol associated tumors comprising the administration of an effective amount of a compound according to any one of claims 1 to 12 to a mammal in need thereof.

17. A pharmaceutical formulation comprising a compound according to any one of claims 1 to 12 in admixture with pharmaceutically acceptable adjuvants, diluents and/or carriers.

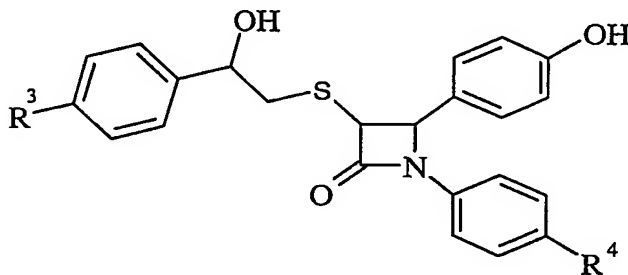
18. A combination of a compound according to formula (I) or (I2) with a PPAR alpha and/or gamma agonist.

10

19. A combination of a compound according to formula (I) or (I2) with an HMG Co-A reductase inhibitor.

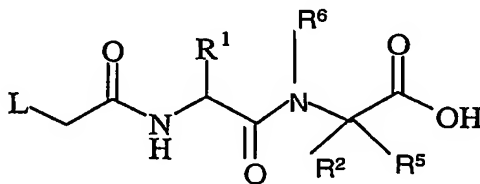
20. A process for preparing a compound of formula (I) or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof which process (wherein variable groups are, unless otherwise specified, as defined in formula (I)) comprises of:

Process 1) reacting a compound of formula (II):



(II)

20 with a compound of formula (III):

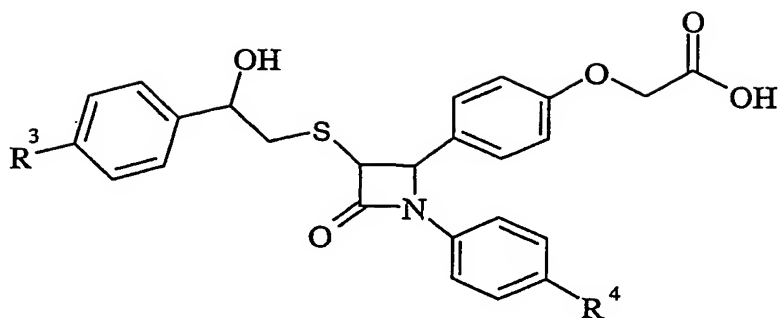


(III)

wherein L is a displaceable group;

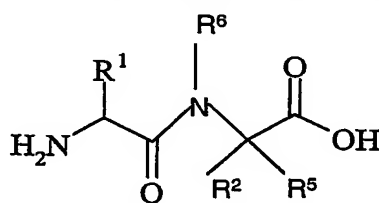
Process 2) reacting an acid of formula (IV):

- 180 -



(IV)

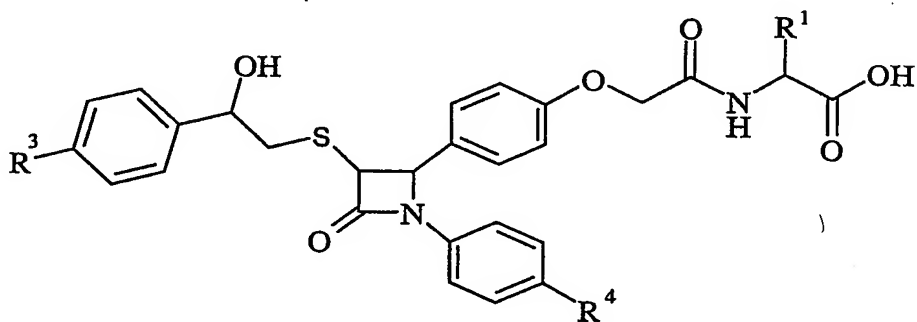
or an activated derivative thereof; with an amine of formula (V):



(V)

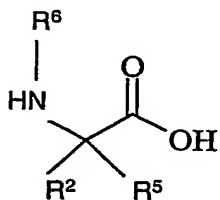
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Process 3): reacting an acid of formula (VI):



(VI)

or an activated derivative thereof, with an amine of formula (VII):

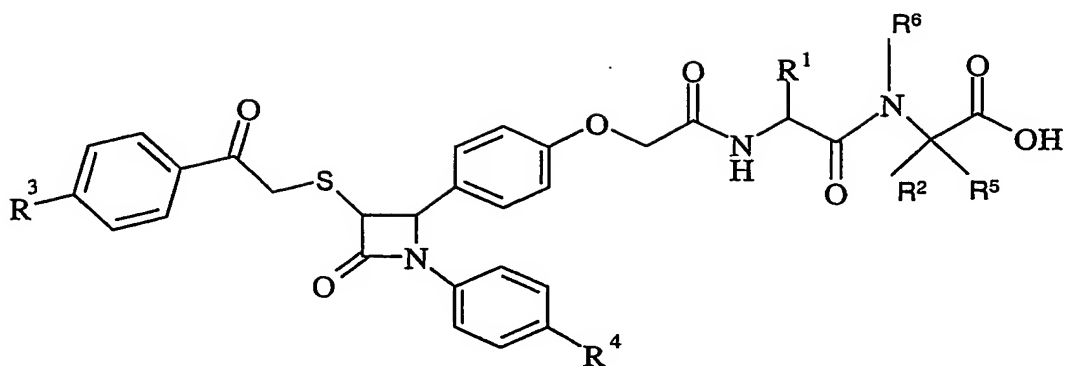


(VII)

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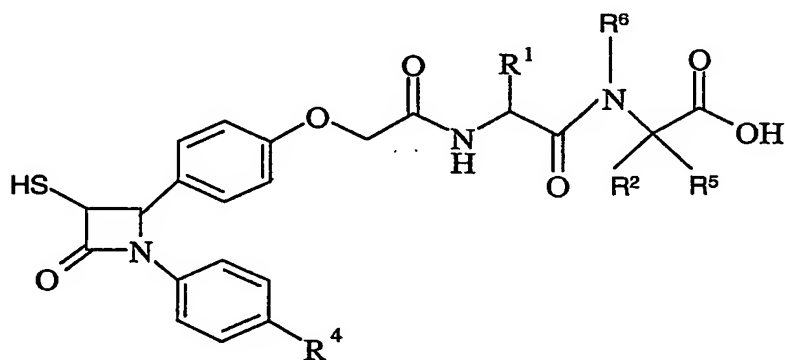
Process 4): reducing a compound of formula (VIII):

- 181 -



(VIII)

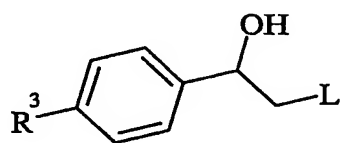
Process 5): reacting a compound of formula (IX):



(IX)

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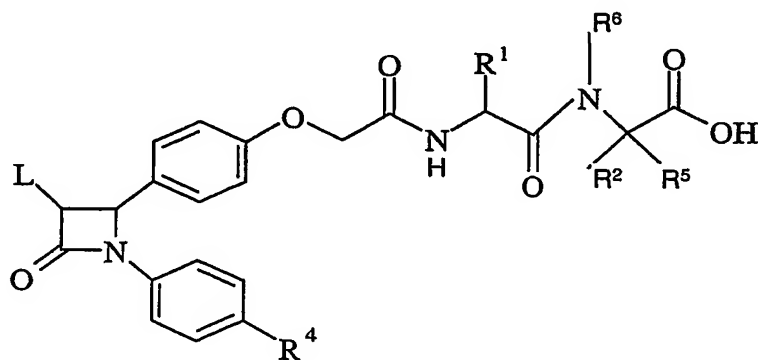
with a compound of formula (X):



(X)

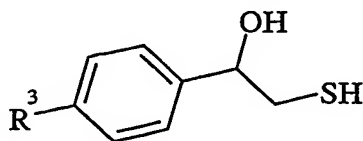
wherein L is a displaceable group;

10 Process 6): reacting a compound of formula (XI):



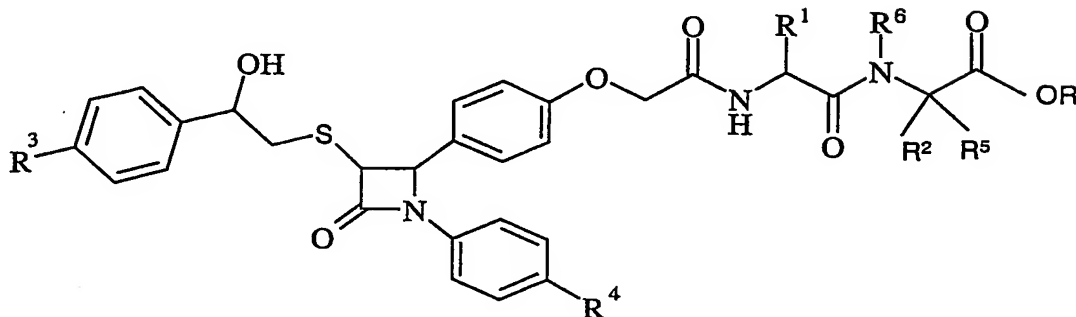
(XI)

wherein L is a displaceable group; with a compound of formula (XII):



(XII)

Process 7): De-esterifying a compound of formula (XIII)



(XIII)

wherein the group C(O)OR is an ester group;

and thereafter if necessary or desirable:

- i) converting a compound of the formula (I) into another compound of the formula (I);
- 10 ii) removing any protecting groups;
- iii) forming a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug; or
- iv) separating two or more enantiomers.

L is a displaceable group, suitable values for L are for example, a halogeno or sulphonyloxy group, for example a chloro, bromo, methanesulphonyloxy or
 15 toluene-4-sulphonyloxy group.

C(O)OR is an ester group, suitable values for C(O)OR are methoxycarbonyl, ethoxycarbonyl, *t*-butoxycarbonyl and benzyloxycarbonyl.